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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,223	07/30/2003	Francis Michon	20695C-001410US	8301

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/630,223	MICHON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *12-41,47-51 and 53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,42-46 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07/30/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *31604 & 71805*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of preliminary amendments filed 08/10/06 and 08/22/06.

Election

2) Acknowledgment is made of Applicants' election filed 08/30/06 in response to the restriction requirement mailed 05/10/06. Applicants have elected invention I with traverse, claims 6-11 and 44-46, and the multivalent GBS conjugate species (a) types Ia, III and V, and the C beta carrier protein species. Applicants' traversal is on the grounds that there are two criteria for a proper requirement for restriction between patentably distinct inventions according to MPEP § 803: (a) The inventions must be independent or distinct as claimed, and (b) There must be serious burden if restriction is not required. Applicants state that all groups of restricted claims are properly presented in the same application; undue diverse searching would not be required; and all claims should be examined together. Applicants allege that the Office has not shown that examination of all the pending claims would require undue searching and/or place a serious burden on the Office, which is a requisite showing for proper issuance of a restriction requirement. Applicants submit that a conjugate molecule and a method of using the conjugate would not be unduly burdensome. Applicants contend that inventions I and II as well as inventions III and IV respectively, are classified in the same class (424) and subclass (197.1) and class (536) and subclass (124), and that there should not be a serious burden to search these claims together. Applicants state that claims of invention I and claims of inventions III and I, as well as claims of invention II and claims of inventions IV and VI should be examined together because there would be overlap, but not a serious burden. Applicants cite MPEP § 803.02 and case law, and traverse the species election requirement. Applicants submit that the PTO cannot require an applicant under the guise of § 121 to divide up the embodiments of a single Markush claim. Applicants state that the art and the USPTO have clearly recognized that groups of specific polysaccharides and/or carrier proteins are often considered together as the mechanism of eliciting a thymus dependent immune response, and is applicable to a wide variety of polysaccharides and carrier proteins.

Applicants' arguments have been carefully considered, but are not fully persuasive. Contrary to Applicants' assertion, in the restriction requirement mailed 05/10/06, the Office clearly established as per MPEP § 803 that the various inventions identified therein are independent or

distinct, and that there is a serious search burden. As set forth therein (see paragraphs 3 and 4 of the restriction requirement), inventions I and II are drawn to two divergent products: a multivalent conjugate comprising GBS capsular polysaccharides, and a multivalent conjugate comprising *N. meningitidis* capsular polysaccharides, which are distinct from one another in their structure, immunospecificity, and functions. Inventions III, IV, V and VI are drawn to different methods, which differ at least in the diverse products used therein. The Office clearly showed therein that the structurally distinct polysaccharides of GBS types Ia, Ib, II, III, V and VIII, and the structurally distinct polysaccharides of A, B, C, W135 and Y *N. meningitidis* capsular polysaccharides require separate individual structural searches. Searching inventions I and II together would impose a serious search burden, since the structure searches are non-coextensive. Applicants should note that despite the same class or subclass indicated, one structure search in patent literature would not be co-extensive to the other due to the divergent structure of the capsular polysaccharides of both inventions. Additionally, there is also search burden with regard to the non-patent literature, which extends beyond the class and subclass searches. Contrary to Applicants' allegation, the Office further showed that searching inventions I and V, and inventions II and VI, would impose a serious search burden due to their separate status in the art as shown by their different classifications. The Office stated therein that a search for these inventions would require a text search for the claimed methods in addition to a search for each product, and that even if each product were known, the methods which use the products, may be novel and unobvious in view of the preamble or active steps. A patent disclosing the claimed product need not and does not always disclose a method of using or making the product. The restriction requirement mailed 05/10/06 is proper and is hereby maintained. Applicants should note that as set forth in paragraphs 7 and 8 of the restriction requirement, if the elected product claims are subsequently found allowable, the withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claims would be rejoined in accordance with the provisions of MPEP § 821.04.

With regard to Applicants' arguments on the species election requirement, Applicants should note that upon further consideration, the species election requirement held between the two multivalent GBS conjugate species is withdrawn, and the product claims 6 and 44 have been examined together with claims 7 and 45. The rest of the species election requirement set forth therein is proper due to the burdensome searches needed because of the structural diversity of the

Markush species identified therein. Contrary to Applicants' assertion, the Markush species are not searched solely based on their common function or mechanism of eliciting a thymus dependent immune response and their applicability to a wide variety of polysaccharides and carrier proteins. In the instant application, a search for one polysaccharide species or carrier protein species is not co-extensive to the other due to the structural divergence or distinctness. The species election requirement set forth is proper and is hereby maintained.

Status of Claims

3) Claims 1-55 are pending.

Claims 13, 14, 16-41, 47-51 and 53-55 are withdrawn from consideration as being directed to non-elected inventions or species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 12 and 15, drawn to the non-elected *N. meningitidis* capsular polysaccharide species, were inadvertently indicated as linking claims to be joined with invention I, if elected, in the restriction requirement mailed 05/10/06. The Office regrets this inadvertent error. Claims 12 and 15 are now properly placed in invention II, and are withdrawn from consideration as being directed to non-elected invention or species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

In addition to the elected C beta carrier protein species, the examination has been extended to one other carrier protein species, tetanus toxoid.

Claims 6-11 and 44-46, and linking claims 1-5, 42, 43 and 52 are under examination.

Information Disclosure Statements

4) Acknowledgment is made of Applicants' Information Disclosure Statements filed 03/16/04 and 07/18/05. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

5) The instant application claims priority to the U.S. provisional application 60/399,949 filed 07/30/2002.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

6) Claim 52 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. This is a new matter rejection.

New claim 52 depends from claim 1 and includes the limitations: 'of claim 1, wherein the polysaccharides are less than 100 kilodaltons in molecular weight'. Applicants point to paragraphs 41 and 49 of the specification as providing support for the new claim 52. However, paragraph 41 describes 'purified' oligosaccharide or bacterial capsular polysaccharide, or fragments of it having a molecular weight "above 100,000". This does not provide descriptive support for the above-identified limitations in claim 52 because the polysaccharides recited in claim 52 are not 'purified' and are 'less than 100' kilodaltons in molecular weight. Therefore, the above-identified new limitations in the claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed by pointing to specific lines and pages, for the new limitations, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

7) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

8) Claims 2-4, 7, 8, 45 and 46 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 2-4 are vague, indefinite, confusing, and appear to lack proper antecedent basis in the limitations: 'different bacterial capsular polysaccharides'. Claims 2-4 depend from claim 1, which already recites 'at least three different bacterial capsular polysaccharides'. Are the 'different bacterial capsular polysaccharides' recited in dependent claims 2-4 different from the ones recited in the base claim 1?

(b) Claims 7 and 45 are indefinite, confusing, and/or inconsistent in the limitations 'type 1a' and 'type Ia' respectively. It is unclear how one differs from the other in terms of scope or

1a' and 'type Ia' respectively. It is unclear how one differs from the other in terms of scope or structure.

(c) Claims 8 and 46, which depend from claims 8 and 45 respectively, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

9) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10) Claims 1, 5, 6, 11 and 42-44 are rejected under 35 U.S.C. § 102(b) as being anticipated by Michon *et al.* (*In*: *Streptococci and the Host.* (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997) (Michon *et al.*, 1997).

Michon *et al.* (1997) disclosed a multivalent conjugate vaccine (i.e., pharmaceutical composition) comprising a beta C protein carrier or tetanus toxoid protein carrier with at least three different Group B *Streptococcus* capsular polysaccharides from types Ia, II and III conjugated to, wherein the conjugate vaccine elicited protective antibodies as tested using a modified neonatal mouse model. The vaccine comprises PBS (i.e., pharmacological acceptable carrier), aluminum hydroxide, and 2 micrograms of each conjugated polysaccharide, i.e., an amount sufficient to elicit protective antibodies against the different capsular polysaccharides. The capsular polysaccharides in the conjugate are oxidized with sodium periodate under controlled conditions to obtain degrees of oxidation in the range of 0.3 to 0.5. See sections 2.1, 2.2, 3, and 4; and Figure 3.

Claims 1, 5, 6, 11 and 42-44 are anticipated by Michon *et al.* (1997).

11) Claims 1, 2, 5, 6, 10, 11 and 42-44 are rejected under 35 U.S.C. § 102(b) as being anticipated by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994 – Applicants' IDS).

Paoletti *et al.* taught a multivalent conjugate vaccine comprising the capsular polysaccharides of Group B streptococcal types Ia, Ib, II and III covalently linked to tetanus toxoid via a selected number of sialic acid residues. The vaccine comprised PBS (i.e., pharmacological

acceptable carrier), Alhydrogel adjuvant, and 2 micrograms of each conjugate, i.e., an amount sufficient to elicit protective antibodies against the different capsular polysaccharides. The conjugate had 7-29% of the sialic acid residues oxidized as sites for protein coupling. The vaccine elicited protective antibodies against the capsular polysaccharides as evaluated using a mouse maternal immunization-neonatal challenge model of GBS infection. The capsular polysaccharides in the tetravalent conjugate vaccine have a size of 200,000 and $>10^6$ *Mr*. See abstract; Materials and Methods; Tables 1, 2, 5 and 6; Figure 1; and pages 3237 and 3238.

Claims 1, 2, 5, 6, 10, 11 and 42-44 are anticipated by Paoletti *et al.*

Rejection(s) under 35 U.S.C. § 103

12) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

13) Claims 9 and 52 are rejected under 35 U.S.C. § 102(b) as being anticipated by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994 – Applicants' IDS) as applied to claims 6 and/or 1 above, and further in view of Wang *et al.* (*PNAS* 95: 6584-6589, 1998).

The teachings of Paoletti *et al.* are explained above which do not expressly teach that the capsular polysaccharides in their glycoconjugate are of a size between 80 and 120 kilodaltons or less than 100 kilodaltons.

However, the depolymerised GBS capsular polysaccharides of desired size, including those that fall in the range between 80 and 120 kilodaltons, or less than 100 kilodaltons were known in the

art at the time of the invention. For instance, Wang *et al.* taught the selectively depolymerised GBS types I-VIII capsular polysaccharides of desired size obtained by controlled treatment of the full-length capsular polysaccharides with ozone, without affecting the labile sialic acid residues of the polysaccharides. Two specific sized capsular polysaccharides obtained were of the size 115 kDa or 61 kDa. Wang *et al.* taught of the art-known, frequently proven preference for short-chain polymers or oligomer fragments of capsular polysaccharides of pathogenic microorganisms including Group B *Streptococci,* for used in vaccine applications. See abstract; 'Materials and Methods'; section 'Kinetics' on page 6587; first paragraph under 'Results and Discussion'; and left column on page 6584; and page 6588.

Given that depolymerised capsular polysaccharides of GBS types having a size of 115 kDa or 61 kDa and having the intact or unaffected sialic acid residues were already known in the art at the time of the invention as taught by Wang *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace GBS capsular polysaccharides of types Ia, Ib, II and III in Paoletti's multivalent GBS conjugate vaccine with Wang's depolymerised GBS capsular polysaccharides of types Ia, Ib, II and III to produce the multivalent conjugate of the instant invention, with a reasonable expectation of success. Given the frequently proven preference for short-chain polymers or oligomer fragments of capsular polysaccharides of pathogenic microorganisms including Group B *Streptococci* for application in vaccines as taught by Wang *et al.*, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS capsular oligosaccharide conjugate for application in vaccines.

Claims 9 and 52 are *prima facie* obvious over the prior art of record.

14) Claims 2, 3, 7, 8, 45 and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Michon *et al.* (*In*: *Streptococci and the Host.* (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997) (Michon *et al.*, 1997) as applied to claims 6, 1 and 42 above and further in view of Michon *et al.* (US 6,602,508) ('508) and Laude-Sharp *et al.* (*In*: *Abstracts of the 97th General Meeting of the American Society for Microbiology*, Miami Beach, FL, page 251, # E-62, 1997).

The reference of Michon *et al.* ('508) is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

The teachings of Michon *et al.* (1997) are explained above, which do not expressly disclose that their multivalent GBS conjugate vaccine composition comprises GBS type V capsular polysaccharide, or five different GBS capsular polysaccharides covalently linked to C beta protein carrier.

However, Michon *et al.* ('508) expressly contemplated multivalent GBS conjugates and vaccines comprising the multivalent conjugates, wherein different types of GBS capsular polysaccharides including types I, II, III, IV and V are conjugated to a single protein, such as beta-C protein of type Ia/Ib Group B streptococcus. Michon *et al.* ('508) taught a method of preparing such conjugates and vaccines. See first and third full paragraphs in column 9; Examples; and claims 16, 22, 26 and 27.

Laude-Sharp *et al.* taught the advantages of using streptococcal C-beta protein as a carrier protein in a combination conjugate vaccine against multiple serotypes of Group B *Streptococcus*. Laude-Sharp *et al.* conjugated the streptococcal C-beta protein to the capsular polysaccharides of different types of GBS, Ia, II and III, and showed that besides its carrier function, the C beta protein afforded protection against GBS strains not covered by capsular polysaccharides in the vaccine. In addition to providing protection against GBS types Ia, II and III, the conjugate vaccine provided additional protection against GBS type Ib. See title and entire disclosure.

Given Michon's ('508) express contemplation of multivalent GBS capsular polysaccharide conjugates and vaccines, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add to Michon's (1997) multivalent conjugate vaccine comprising GBS types Ia, II and III conjugated to beta C protein GBS type IV and V capsular polysaccharides conjugated to C beta protein produced using the conjugation method of Michon *et al.* ('508) or Michon *et al.* (1997) to produce the tetravalent or the pentavalent GBS conjugate vaccine of the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of producing a multivalent GBS conjugate vaccine wherein five different GBS type capsular polysaccharides are conjugated to streptococcal beta C protein, which multivalent conjugate not only advantageously confers immunity against multiple GBS types I, II, III, IV and V, but also affords protection via C-beta protein against GBS strains not covered by the capsular

polysaccharides in the vaccine including GBS type Ib as taught by Laude-Sharp *et al.*

Claims 2, 3, 7, 8, 45 and 46 are *prima facie* obvious over the prior art of record.

15) Claims 1-7 and 42-45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over in view of Jennings *et al.* (US 5,993,825 – Applicants' IDS) ('825) in view of Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994 – Applicants' IDS) and Claesson *et al.* (*J Pediatr.* 114: 97-100, 1989).

It is noted that the recited four, five, or six different bacterial capsular polysaccharides in the dependent claims 2-4 are not required to be 'the at least three bacterial capsular polysaccharides' recited in the base claim 1 and therefore encompass any four, five, or six different bacterial capsular polysaccharides.

Jennings *et al.* ('825) disclosed a multivalent conjugate vaccine comprising Group B *Streptococcus* type II and type V capsular polysaccharides having a size of about 100 kilodaltons covalently linked to a carrier protein such as tetanus toxoid and capable of eliciting opsonophagocytic antibodies and further comprising immunogenic molecules capable of eliciting protective antibodies to pathogens other than GBS type II and type V, such as GBS types Ia, Ib, III and IV, *Haemophilus influenzae* type b, and *E. coli* K1. See abstract; last full paragraph in column 2; paragraph bridging columns 2 and 3; third full paragraph in column 4; Examples; and 'Results'. Jennings *et al.* ('825) also taught a GBS type III conjugate wherein the GBS type III capsular polysaccharide is conjugated to tetanus toxoid and elicited GBS type III-specific opsonically active antibodies (see first full paragraph in column 2).

Jennings *et al.* ('825) do not identify the non-GBS type II immunogenic molecules in their vaccine, i.e., GBS types Ia, Ib, III, IV and V, *Haemophilus influenzae* type b, and *E. coli* K1 immunogenic molecules, as GBS types Ia, Ib, III, IV and V, *Haemophilus influenzae* type b, and *E. coli* K1 capsular polysaccharide-protein conjugates capable of eliciting protective antibodies.

However, non-GBS type II immunogenic conjugate vaccines such as GBS types Ia, Ib, III, IV and V, *Haemophilus influenzae* type b, and *E. coli* K1 conjugate vaccines capable of eliciting protective antibodies, were already known and available in the art at the time of the instant invention. For instance, Paoletti *et al.* taught a multivalent conjugate vaccine comprising the capsular polysaccharides of Group B streptococcal types Ia, Ib, and III covalently linked to tetanus toxoid via a selected number of sialic acid residues. The vaccine comprised PBS (i.e., pharmacological acceptable carrier), Alhydrogel adjuvant, and 2 micrograms of each conjugate, i.e.,

an amount sufficient to elicit protective antibodies against the different capsular polysaccharides. The conjugate had 7-29% of the sialic acid residues oxidized as sites for protein coupling. The vaccine elicited protective antibodies against the capsular polysaccharides as evaluated using a mouse maternal immunization-neonatal challenge model of GBS infection. The capsular polysaccharides in the tetravalent conjugate vaccine have a size of 200,000 and $>10^6$ *Mr*. See abstract; Materials and Methods; Tables 1, 2, 5 and 6; Figure 1; and pages 3237 and 3238.

Similarly, a conjugate vaccine comprising *Haemophilus influenzae* type b capsular polysaccharide covalently linked to tetanus toxoid and being capable of eliciting protective antibodies to *Haemophilus influenzae* type was already known and available in the art at the time of the invention. For instance, Claesson *et al.* taught such a conjugate vaccine comprising *Haemophilus influenzae* type b capsular polysaccharide covalently linked to tetanus toxoid that induces protective level of antibodies against *Haemophilus influenzae* type b. See title; 'Methods'; 'Results'; and page 99.

Given Jennings' ('825) express teaching of including, in a multivalent conjugate vaccine composition comprising Group B streptococcus type II and type V capsular polysaccharides covalently linked to a carrier protein such as tetanus toxoid and capable of eliciting opsonophagocytic antibodies, further immunogenic molecules capable of eliciting protective antibodies to pathogens other than GBS type II and type V, such as GBS types Ia, Ib, and III, *Haemophilus influenzae* type b, and *E. coli* K1, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a multivalent conjugate vaccine composition by combining Jennings' ('825) GBS capsular type II-TT and type V-TT conjugates with Paoletti's GBS conjugate comprising GBS types Ia, Ib, and III conjugated to TT and Claesson's protective conjugate comprising *Haemophilus influenzae* type b capsular polysaccharide covalently linked to tetanus toxoid to produce the multivalent conjugate vaccine composition of the instant invention with a reasonable expectation of success. Given the express teachings of Jennings *et al.* ('825) of including GBS non-type type II and type V capsular conjugates in their multivalent conjugate vaccine composition other immunogenic molecules capable of eliciting protective antibodies to pathogens other than GBS type II and type V, such as GBS types Ia, Ib, and III, *Haemophilus influenzae* type b, and *E. coli* K1, one of ordinary skill in the

art would have been motivated to produce the instant invention for the expected benefit of providing a single multivalent conjugate vaccine that advantageously provides protection against other pathogenic serotypes of GBS such as Ia, Ib, and III in addition to GBS types II and III, and also against the known non-GBS pathogen *Haemophilus influenzae* type b.

Claims 1-7 and 42-45 are *prima facie* obvious over the prior art of record.

Objection(s)

16) Claims 8 and 42 are objected to for the following reasons:

(a) Claim 8 is objected to for lacking a period at the end of the claim.

(b) Claim 42 is objected to for the incorrect limitation: 'multiv alent' (see line 4).

Relevant Prior Art

17) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Chong *et al.* (WO 99/42130) disclosed a multivalent immunogenic molecule comprising multiple purified capsular polysaccharides or oligosaccharides (i.e., depolymerized polysaccharides) of *Neisseria meningitidis* derived from serogroup A, C, W-135 and Y, each linked to a carrier protein for use as a medicament against meningitis. See claims 1, 6-8, 39 and 40; paragraph bridging pages 9 and 10; pages 10 and 12; and Examples 1, 2 and 4.

- Ryall (US 2003/0068336 A1) taught a combined or multivalent vaccine comprising four distinct polysaccharide-protein conjugates wherein the capsular polysaccharides from *Neisseria meningitidis* serogroups A, C, W-135, and Y are conjugated to a protein carrier. See abstract and claims.

Remarks

18) Claims 1-11, 42-46 and 52 stand rejected.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Central Fax number, (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

20) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Action supervisor, Albert Navarro, can be reached on (571) 272-0861.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

October, 2006

S. DEVI, PH.D.
PRIMARY EXAMINER